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CANCER DIAGNOSTICS

# NOVITAS LCD INVESTOR PRESENTATION

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**13 January 2025**

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# PACIFIC EDGE'S MEDICARE JOURNEY

**July '20**

Novitas informs Pacific Edge that Cxbladder is covered (A58529, retired Nov '22)

**July '22**

Novitas proposes non-coverage for Cxbladder with LCD (DL39365)

Implementation seen as unlikely

**July - Sep '22**

Open Meetings, Public Comment. Support from industry, patient advocates & customers to retire/revise DL39365

**Sep 22 - May '23**

Contingency planning for adverse LCD determination amid expectation of continued coverage

**Jan '23**

Triage gains coding and reimbursement under LCA (A58917)

**June '23**

Novitas finalizes LCD (L39365) with non-coverage for Cxbladder, future effective on 17 July

**June - July '23**

We pursue all legal and political strategies to overturn the LCD

**July '23**

Novitas agrees to follow procedure for notice and comment on the LCD

LCD stayed, Medicare coverage continues

**Aug '23 – May '24**

Participated in Novitas' open notice & comment process

Engaged with CMS

Published STRATA

Novitas agrees to review PPT & STRATA

**July '24**

CMS grants an extension to Novitas to ensure all comments can be considered

**Aug '24**

Published AV Paper on all existing Cxbladder products

Novitas agrees to review

**Aug '24**

C21 and other stakeholders meet with CMS regarding Extension

**Jan '25**

Novitas finalizes LCD under a new name: 'Genetic Testing in Oncology: Specific Tests' (L39365)'

*Novitas is the Medicare Administrative Contactor (MAC) with jurisdiction for Pacific Edge's US laboratory.*

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# ‘GENETIC TESTING IN ONCOLOGY: SPECIFIC TESTS’ (L39365)

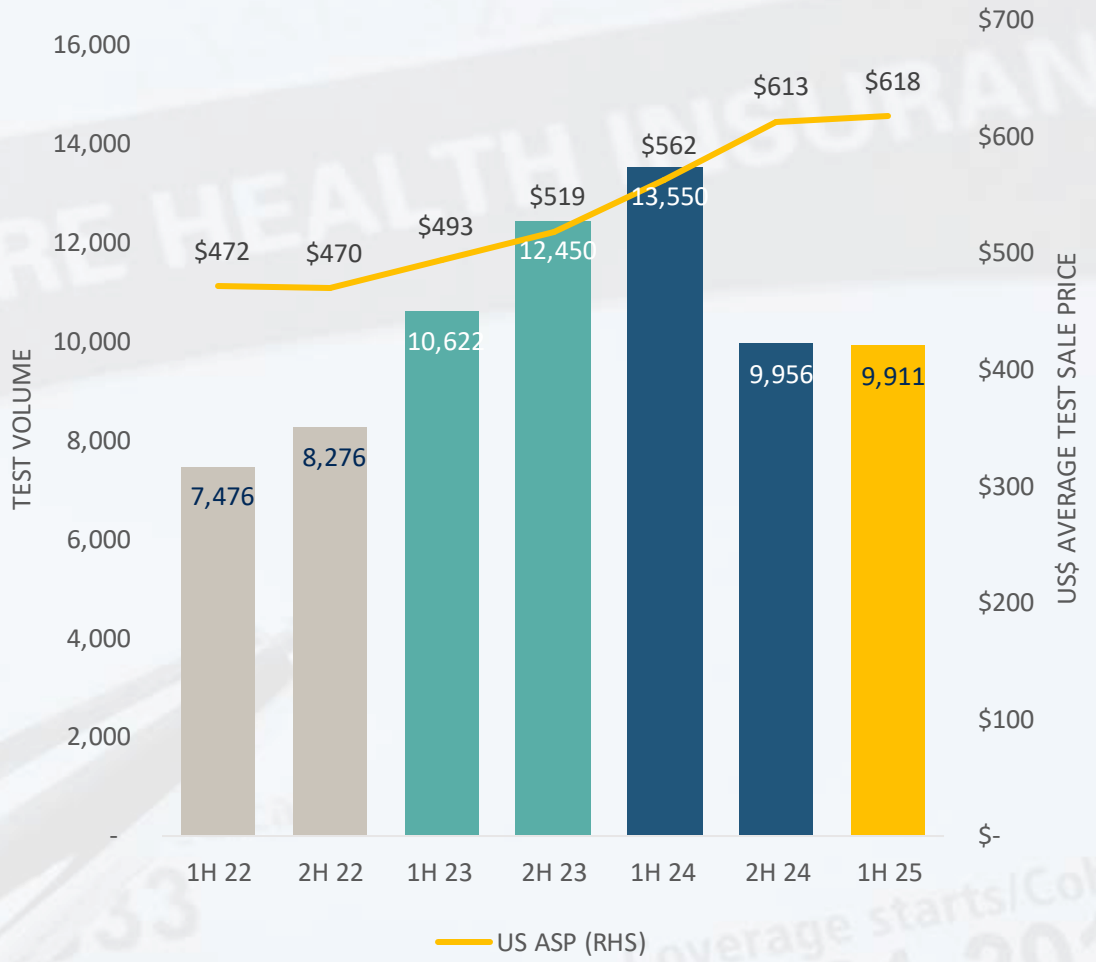
## FINDINGS

- Finalized LCD no longer relies on 3rd party databases/compendia
- Finalized LCD no longer preemptively non-covers non-commercial tests
- Finalized LCD has been reduced to an evidentiary review and non-coverage determination of specific tests including Cxbladder, concluding that “Cxbladder tests are not reasonable and necessary to support positive outcomes in the management of bladder cancer”
- Finalized LCD repeats concerns detailed in the original draft:
  - Conflates hematuria evaluation with screening
  - Insufficient validation in confounding clinical circumstances
  - Low PPV and high numbers of false positives
  - Questions credibility of Pacific Edge funded research

## MEDICARE IS PACIFIC EDGE’S LARGEST PAYER

- Medicare and Medicare Advantage is the largest global opportunity in bladder cancer diagnostics from a single coverage decision
- In 1H 25 Medicare and Medicare Advantage delivered ~5,300 commercial tests (~54% of US commercial tests) and ~$6.5m NZD in total operating revenue (~59% of total operating revenue)
- Pacific Edge expects to be reimbursed at US$760/test until 23 February 2025

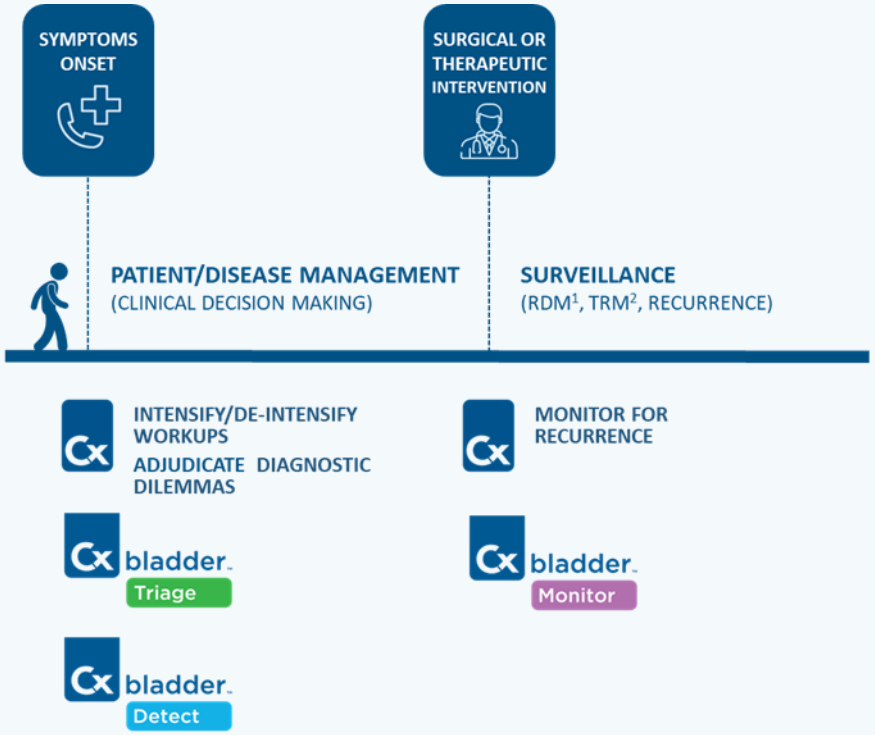
## US COMMERCIAL TEST VOLUMES AND ASP* (US$)




1. Novitas is the Medicare Administrative Contractor for Pacific Edge’s US laboratory. It is empowered by the Centers for Medicare and Medicaid Services (CMS) to make the coverage determination, but it is accountable to CMS for the decision.

# NOVITAS CONTINUES TO MISUNDERSTAND THE VALUE OF CXBLADDER

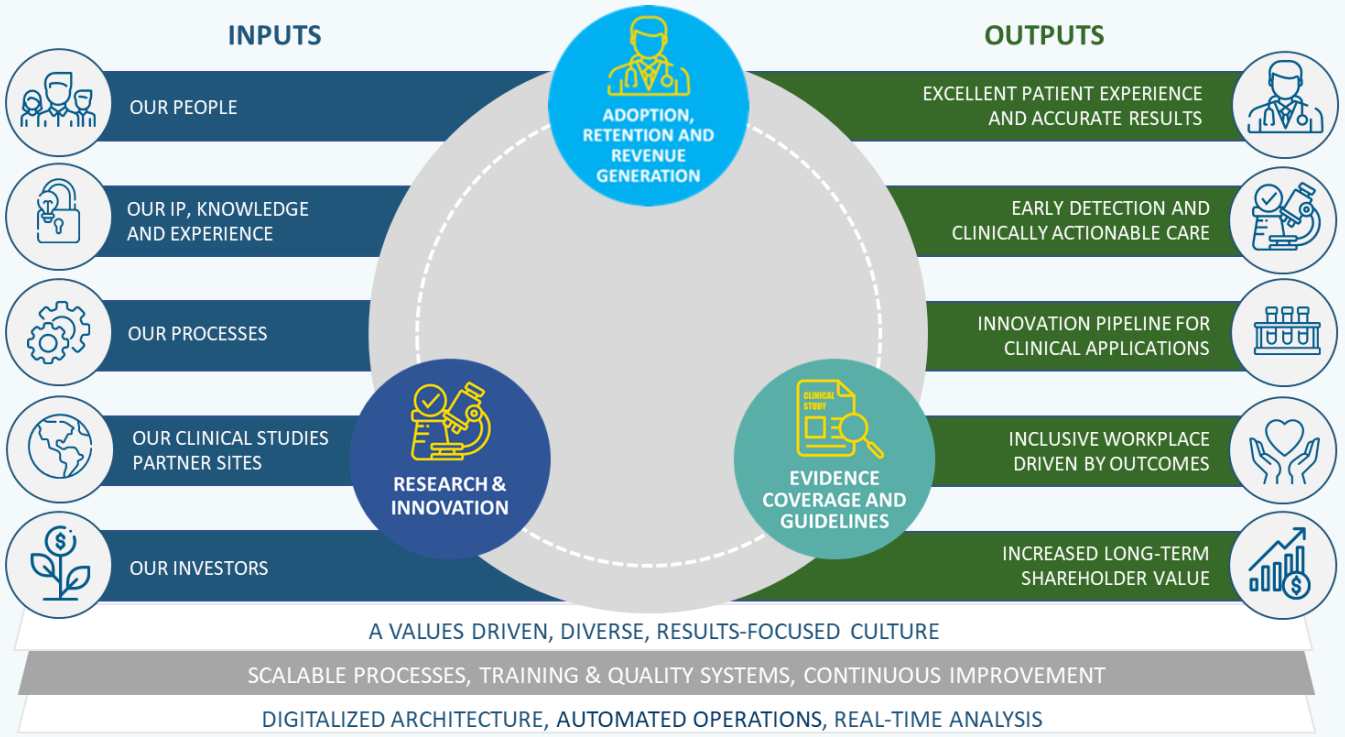
- Appears to misunderstand the intended patient population and the important role that biomarkers can play in risk stratifying hematuria patients
  - Appears to assume Cxbladder products are a screening test
- Fails to consider new peer reviewed evidence, despite notifying Pacific Edge in writing that it would incorporate that evidence:
  - the STRATA[1] randomized control study published in July 2024, which demonstrated the Clinical Utility (CU) of Cxbladder Triage
  - the analytical validation data of Cxbladder Detect, Triage and Monitor published in September 2024
- Does not acknowledge:
  - A Journal of Urology editorial noting the clinical value of Cxbladder
  - Representations on the draft LCD calling for calling for continued Medicare coverage of Cxbladder during the 'Notice and Comment' period in 2023
    - the American Urological Association (AUA)
    - the Large Urology Group Practice Association (LUGPA), and
    - the American Association of Clinical Urologists (AACU)
    - Coalition for 21st Century Medicine (C21), and
    - the American Clinical Laboratory Association (ACLA)
- Repeats its flawed analysis of the existing Cxbladder test evidence by focusing on the biomarker discovery study by Holyoake et al in 2008[4] and creates confounded conclusions by lumping the evidence in future publications from all assays together
- Does not explicitly clarify whether hematuria is or is not substantiated suspicion of disease
  - If not, LCD should have no scope to non-cover non-oncologic tests like Triage and Detect





1. Lotan et al (2024). A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. J Urol 2024.
2. Harvey et al (2024) Analytical Validation of Cxbladder® Detect, Triage, and Monitor: Assays for Detection and Management of Urothelial Carcinoma. Diagnostics. 2024; 14(18):2061.
3. Anderson C. (2024) What Is the Future of Cystoscopy for Detecting Urothelial Carcinoma? J Urol. Vol. 212, 399-400, September 2024.
4. Holyoake et al (2008) Development of a multiplex RNA urine test for the detection and stratification of transitional cell carcinoma of the bladder. Clin Cancer Res 2008;14:742–9.

# VALUE CREATION THROUGH A FOCUS ON THREE PILLARS




## WE PREPARED FOR THIS OUTCOME

- We have re-focused the business on clinical development for guidelines inclusion and increased coverage certainty for Detect Plus & Monitor Plus
- We have restructured our commercial operations to focus on profitable territories
- We have adjusted our selling focus towards the clinical value of Cxbladder as the driver of higher throughput/headcount and throughput/clinician and health economics messaging
- The company is well placed to fund the re-coverage process if necessary and regain reimbursement for our tests

# SETTING A ROUTE TO REGAINING MEDICARE COVERAGE

## ACTIVATING OUR CONTINGENCY PLANS

- Potential legal challenge to the LCD on procedural and fairness grounds
- Further review the structure of our operations and our strategy to reduce cash burn in line with our plan to regain Medicare coverage
- Submit a reconsideration request to Novitas regarding the evidence not already considered of the Journal of Urology's publication of the STRATA[1] study and the updated Analytical Validation studies of Triage, Detect and Monitor[2]
- Continue to advance our clinical evidence generation program in an AV/CV/CU framework for Guidelines inclusion by the AUA and NCCN
- Continue to publish evidence from our partnership with Kaiser Permanente
- Continue to explore other strategic alternatives for Pacific Edge that could support the company through regaining Medicare coverage and advancing the commercialization of Cxbladder globally



1. Lotan et al (2024). A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. J Urol 2024.
2. Harvey et al (2024) Analytical Validation of Cxbladder® Detect, Triage, and Monitor: Assays for Detection and Management of Urothelial Carcinoma. Diagnostics. 2024; 14(18):2061.

# CLINICAL EVIDENCE CATALYSTS FOR COVERAGE CERTAINTY

## MEDICARE RECONSIDERATION AND GUIDELINE INCLUSION REQUESTS

**(Novitas[1] typically handles reconsideration requests on existing LCDs within three months of submission)**

| Catalyst | Test and evidence standard [2] | Expected date of reconsideration request [3] |
|---|---|---|
| **1. STRATA data published** | - CU of Triage | Novitas notified of the publication in April |
| **2. Automated RNA and DNA extraction** | - AV of Triage, Detect and Monitor | Q3 2024 (Published September, Novitas notified) |
| **3. Triage Plus Analytical Validation** | - AV of Triage Plus | Q2 2025 |
| **4. DRIVE data published** | - CV of Triage Plus | Q2 2025 |
| **5. STRATA concordance** | - CU of Triage Plus (concordance) | Q3 2025 |
| **6. Kaiser Permanente RWE[4] published** | - CU of Triage (RWE) | Q3 2025[5] |
| **7. AUSSIE data published** | - CV of Triage Plus | Q4 2025 |
| **8. microDRIVE published** | - CV of Triage Plus | Q1 2026 |
| **9. Monitor Plus Analytical Validation** | - AV of Monitor Plus | Q2 2026 |
| **10. Pooled CV data published[6]** | - CV of Triage Plus | Q2 2026 |
| **11. LOBSTER published** | - CV of Monitor/Monitor Plus | Q1 2027 |
| **12. CREDIBLE data published** | - CU of Triage Plus | Q3 2027 |

[1] Novitas is the Medicare Administrative Contractor (MAC) charged with making the Medicare local coverage determination for Pacific Edge's US laboratory

[2] AV, CV CU, respectively Analytical Validity, Clinical Validity, Clinical Utility

[3] All dates are calendar year rather than financial year and our best current estimates

[4] RWE is Real World Evidence

[5] Timeline determined by Kaiser Permanente

[6] The pooled analysis brings together data from DRIVE, AUSSIE and microDRIVE

*Pacific Edge will also lodge a reconsideration request if Cxbladder is included in the American Urological Association (AUA) or National Comprehensive Cancer Network (NCCN) guidelines*

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# INDEPENDENT REAL-WORLD EVIDENCE OF CXBLADDER'S CLINICAL UTLITY

## CLINICAL UTILITY EVIDENCE OF CXBLADDER TRIAGE THAT SUPPORTS MEDICARE COVERAGE

### KAISER PERMANENTE ABSTRACT SHOWS CLINICAL VALUE IN REAL WORLD SETTING

- Kaiser Permanente presented an abstract to the Western Section AUA conference regarding their ongoing experience with Cxbladder Triage
- The abstract focuses on 1,563 low-risk patients in the Kaiser Southern California health system with no history of gross hematuria or who refused cystoscopy
  - 1,200 patients avoided invasive cystoscopy, improving patient satisfaction, urology access and lowering the overall cost of care
- A peer-reviewed publication is expected on the complete data set, targeting the AUA conference in 2025
- Pacific Edge will use this future publication for a Medicare reconsideration request (in the event of a non-coverage determination)

KAISER PERMANENTE®

**1,563**
Low-risk patients took a Cxbladder Triage test
**Patients**:
- Had no history of gross hematuria; or
- Refused cystoscopy

**1,200 (77%)**
NEGATIVE RESULT
Avoided a cystoscopy

**363 (23%)**
POSITIVE RESULT
Identified as 'high-risk' of cancer

**310**
Underwent a cystoscopy

**19**
Diagnosed with cancer (6.1% of those examined)

*"Incorporating a highly reliable urine biomarker into clinical workflows for hematuria reduced the burden of cystoscopy substantially, improving patient satisfaction, urology access, and lowering overall cost of care,"*
*- Loo et al (2024)[1]*

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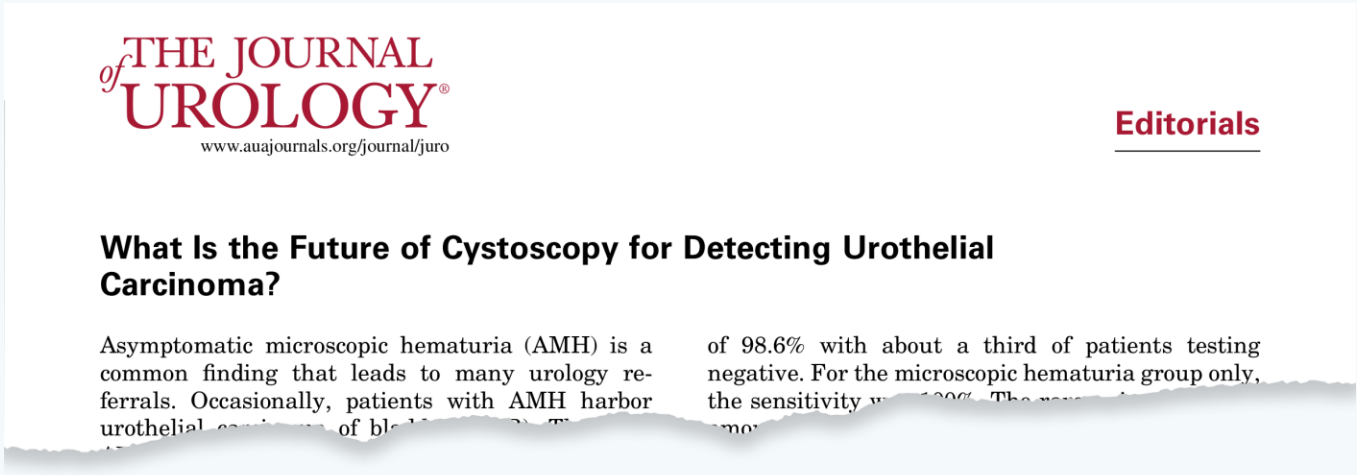
[1] Real World Clinical Utility of a Urinary Biomarker (Cxbladder Triage) for Hematuria Referrals in an Integrated Managed Care Health System. Abstract accepted for presentation to the Western Section of the American Urological Association annual conference.

# AUA HEMATURIA GUIDELINES – A COMPREHENSIVE REVIEW

## AN APPROACH THAT SUPPORTS OUR DRIVE FOR GUIDELINE INCLUSION

- The AUA has commenced a review of the microhematuria guideline and has asked for professional comment on its initial draft; no timeframe provided
- The clinical utility of Cxbladder Triage demonstrated by the STRATA[1] study is expected to be considered as part of the deliberations
- A positive AUA Journal of Urology editorial in July 2024 suggests favorable direction of travel
- Clear/positive inclusion language would be used as the basis for a Medicare coverage re-consideration request (in the event of a non-coverage determination)



THE JOURNAL of UROLOGY®
www.auajournals.org/journal/juro

Editorials

**What Is the Future of Cystoscopy for Detecting Urothelial Carcinoma?**

Asymptomatic microscopic hematuria (AMH) is a common finding that leads to many urology referrals. Occasionally, patients with AMH harbor urothelial [illegible] of bl[illegible]

of 98.6% with about a third of patients testing negative. For the microscopic hematuria group only, the sensitivity w[illegible]

American Urological Association

**www.auanet.org**

- Globally the most influential and largest urological association
- **Relevant standards of care**: Hematuria, microhematuria management and non-muscle invasive bladder cancer (NMIBC)
- **Review period**: with new evidence, last updated in 2020

*"… these tests have the potential to improve the management of our patients with suspected [urothelial cancer] who would otherwise require an invasive procedure for diagnosis."*

*– Journal of Urology editorial Sept 2024*

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1. Lotan et al. (2024) . A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. The Journal of Urology Vol 212 1-8 Jul 2024.

# SUMMARY AND OUTLOOK

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# OUTLOOK: MORE CATALYSTS THAN HEADWINDS

- We are disappointed with this decision, but have prepared for it
- We will focus on the available legal and appeals avenues in the next 45 days
- We will continue our evidence generation focus until re-coverage
- The company is well placed to fund the re-coverage process if necessary and regain reimbursement for our tests

**HEADWINDS:**

- Customer response to the non-coverage determination
- Negative physician or patient response to expanding the enhanced patient responsibility program

**CATALYSTS:**

- Potential inclusion in the AUA Microhematuria Guidelines
- Reconsideration of already-published Clinical Evidence
  - STRATA publication on the CU of Triage
  - AV publication for Triage, Detect and Monitor
- Reconsideration of new Clinical Evidence
  - AV publication for Triage Plus
  - DRIVE publication for Triage Plus
- Cxbladder Triage Plus pricing via Gapfill
- New clinician-generated CU evidence as studies completed (particularly Kaiser)
- Litigation success

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# APPENDIX

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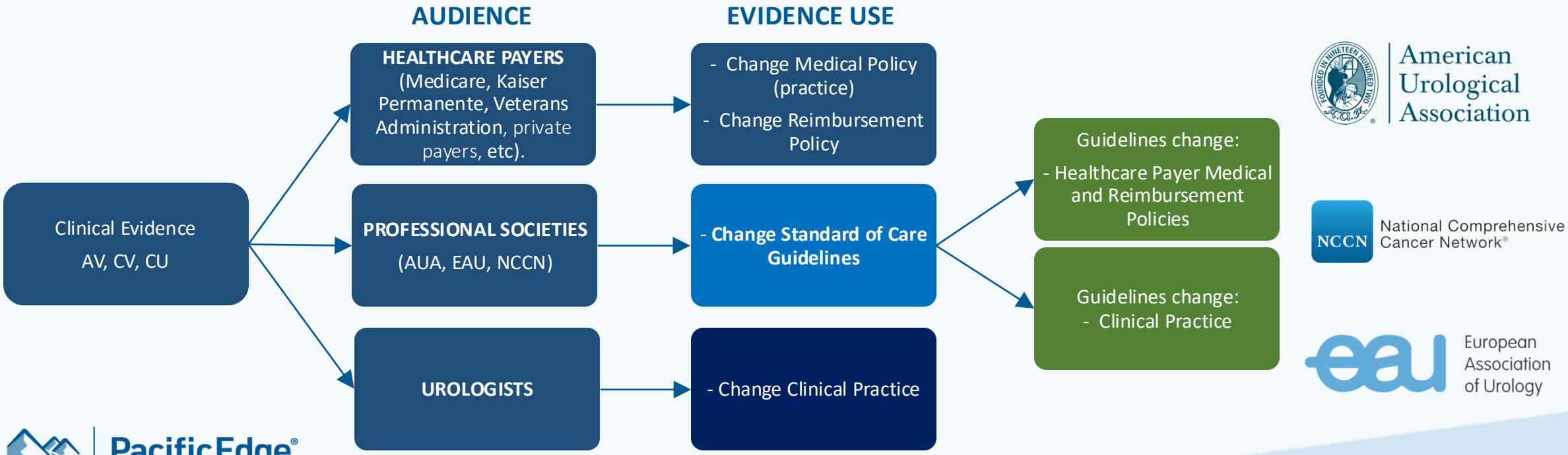
# PACIFIC EDGE'S EVIDENCE PROGRAM SEEKS TO CHANGE CLINICAL PRACTICE

## STRUCTURED CLINICAL EVIDENCE DEVELOPMENT

- Pacific Edge's clinical study program is focused on developing clinical evidence for Cxbladder tests in a structured framework
  - **Analytical Validity (AV)**: Evidence that a test is repeatable in the lab for a given indication and population
  - **Clinical Validity (CV):** Evidence a test works in the same way on an independent eligible population for a given indication
  - **Clinical Utility (CU):** Evidence that a test changes clinical practice in the hands of a physician, typically in prospectively recruited RCTs
  - **Real World Evidence (RWE)**: CU verification of the real-world use of the test in clinical practice, usually through regular use of the test by physicians
- Clinical Utility evidence obtained through randomized control trials is required to change standard of care guidelines (in addition to AV and CV evidence)

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# SUMMARY OF CLINICAL EVIDENCE

| | | Study | Pop. Type | Sensitivity (Sn) | NPV | Specificity (Sp) | Comment |
|---|---|---|---|---|---|---|---|
| **Triage Plus** | **Proof of concept** | Lotan et al., 2022 | MH + GH* | 97% | 99.7% | 90% | Pooled data from US and Singapore cohorts (*n*=804). Called Detect+ in publication. |
| | **CV** | DRIVE (unpublished) (**1**) | MH + GH* | | | | *Study in progress* |
| | | AUSSIE (unpublished) (**4**) | MH + GH* | | | | *Study in progress* |
| | | microDRIVE (unpublished) (**5**) | MH* | | | | *Study in progress* |
| | **CU** | CREDIBLE (not started) **(6)** | MH | | | | *Protocol in final development stages, site selection starting by the end of year.* |
| **Triage** | **AV** | Kavalieris et al., 2015 | MH + GH* | 95.10% | 98.50% | 45% | **Sn, Sp, NPV** values when test-negative rate is 40% |
| | **CV** | Davidson et al., 2019 | MH + GH* | 95.5% (**1**) | 98.6% (**1**) | 34.3% | GH only: **Sn** (95.1%), **NPV** (98%), **Sp** (32.8%); MH only: **Sn** (100%), **NPV** (100%), **Sp** (42.6%) |
| | | Konety et al., 2019 | (**2**) | 100% | | | Cxbladder (**3**) correctly adjudicated all UC confirmed patients (*n*=26) with atypical urine cytology results (*n*=153, **4**) |
| | | Lotan et al., 2022 | MH + GH* | 89% | 99% | 63% | Pooled data from US and Singapore cohorts (*n*=804) |
| | **CU** | Davidson et al., 2020 | MH + GH* | 89.4% (**5**) | 98.9% (**5**) | 59% (**5**) | 39% of patients testing negative for Cxb Triage & imaging did not get cystoscopy & were managed at primary care (**6**) |
| | | Lotan et al., 2024 (**7**) | MH + GH* | 90% | 99% | 56% | Showed clinicians using Triage undertook 59% fewer cystoscopies on low-risk patients presenting with hematuria. |
| **Detect** | **AV** | O'Sullivan et al., 2012 | GH* | 81.8% | 97% | 85.1% | Cxb Detect detected 97% of HG tumors & 100% of Stage 1 or greater tumors |
| | **CV** | Lotan et al., 2022 | MH + GH* | 74% | 97% | 82% | Pooled data from US and Singapore cohorts (*n*=804) |
| | | DRIVE (unpublished) (1) | MH + GH* | | | | *Study in progress* |
| | **Health Economics** | Tyson et al., 2023 | MH | | | | Published economic model shows significant savings for healthcare payers (median savings of $559 in direct costs per patient) |
| **Monitor** | **AV** | Kavalieris et al., 2017 | (**1**) | 88% (**2**) | 97% (**2**) | N/A | (**3**) |
| | **CV** | Konety et al., 2019 | (**4**) | 100% | | | Cxbladder (**5**) correctly adjudicated all UC confirmed patients (*n*=26) with atypical urine cytology results (*n*=153, **6**) |
| | **CU** | Koya et al., 2020 | (**7**) | | | | Integration of Cxb Monitor into the surveillance schedule reduced annual cystoscopies (39%) (8,9) |
| | **CU** | Li et al., 2023 | **(7)** | | | | Cxbladder Monitor safely postpones a patient's next scheduled cystoscopy, the current 'gold standard' for bladder cancer surveillance |

* Referred patients. Definitions - MH: Microhematuria, GH: Gross Hematuria. For Sensitivity, NPV and Specificity please see page 41 of this presentation

# FOOTNOTES FOR CLINICAL EVIDENCE SUMMARY

| | Footnotes | |
|---|---|---|
| **Triage Plus** | 1 | Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Triage Plus). |
| | 2 | Observational study to validate performance characteristics of Cxb Triage Plus in patients with UC of the upper tract. |
| | 3 | Patients with suspected upper tract UC (UTUC) or surveillance patients with a history of UTUC. |
| | 4 | Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Triage Plus). |
| | 5 | Observational study to validate performance characteristics of Cxb Triage Plus in microhematuria (MH) patients. |
| | 6 | Clinical utility study comparing the reduction of cystoscopy use when implementing the new clinical pathway to SOC in a defined MH population. |

| | | |
|---|---|---|
| **Triage** | **1** | Cxb Triage performance; Cxb Triage & imaging combined performance had a **Sn** of 97.7% & **NPV** of 99.8%. |
| | **2** | Patients included hematuria evaluation (*n*=436) or surveillance previously diagnosed with UC (*n*=416) with both Cxbladder & urine cytology results. |
| | **3** | Cxbladder includes Cxbladder Triage & Cxbladder Monitor. |
| | **4** | This included *n*=70 for patients with hematuria & *n*=83 for patients with previously diagnosed UC and overall test negative rate of 30.7%. |
| | **5** | Cxb Triage performance; Cxb Triage & imaging combined performance had a **Sn** of 98.1%, **NPV** of 99.9% & **Sp** of 98.4%. |
| | **6** | Cxb Triage negative rate was 53%; Follow-up period of 21-months showed no missed cancers, demonstrating safety. |
| | **7** | Cxb Triage demonstrated to have clinical utility in safely risk stratifying low risk microhematuria patients and not undertake cystoscopy. |

| | | |
|---|---|---|
| **Detect** | **1** | Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Detect$^{+}$). |

| | | |
|---|---|---|
| **Monitor** | **1** | Surveillance patients previously diagnosed with primary or recurrent UC. |
| | **2** | Cxb Monitor performance characteristics on surveillance patients diagnosed with primary UC; Cxb Monitor had a **Sn** of 93% and **NPV** of 94% on patients with recurrent UC. |
| | **3** | Using Kavalieris et al., (2017) data set, Lotan et al., (2017) compared relative performance of Cxb Monitor against NMP22 ELISA, NMP22 BladderChek and urine cytology. |
| | **4** | Patients included hematuria evaluation (*n*=436) or previously diagnosed UC (*n*=416) with both Cxbladder & urine cytology results. |
| | **5** | Cxbladder includes Cxbladder Triage & Cxbladder Monitor. |
| | **6** | This included *n*=70 for patients with hematuria & *n*=83 for patients with previously diagnosed UC; test negative rate of 30.7%. |
| | **7** | All patients were being evaluated for recurrence of UC (*n*=309 providing 443 samples). |
| | **8** | Cxb Monitor identified all seven confirmed recurrence events idnetified on the first cystoscopy. |
| | **9** | Patients returning negative Cxb Monitor results (n=235) had no pathology-confirmed recurrence at 1st cystoscopy |

# REFERENCES SUMMARY OF CLINICAL EVIDENCE

| | References |
|---|---|
| **Triage Plus** | Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification[1]. The Journal of Urology, 10-1097. |

| | |
|---|---|
| **Triage** | Davidson et al., (2019). Inclusion of a molecular marker of bladder cancer in a clinical pathway for investigation of haematuria may reduce the need for cystoscopy. NZ Med J, 132(1497), 55-64. |
| | Davidson et al., (2020). Assessment of a clinical pathway for investigation of haematuria that reduces the need for cystoscopy. The New Zealand Medical Journal (Online), 133(1527), 71-82. |
| | Kavalieris et al., (2015). A segregation index combining phenotypic (clinical characteristics) and genotypic (gene expression) biomarkers from a urine sample to triage outpatients presenting with hematuria who have a low probability of urothelial carcinoma. BMC urology, 15(1), 1-12. |
| | Konety et al., (2019). Evaluation of Cxbladder and adjudication of atypical cytology and equivocal cystoscopy. European urology, 76(2), 238-243. |
| | Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification. The Journal of Urology, 10-1097. |
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1. Triage Plus was called Detect+ in this publication

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